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JPO Abstracts Database
EPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Term: l1 same l3

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DATE: Monday, November 04, 2002 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=ADJ			
L7	l1 same l3	8	L7
L6	l1 same l2	17	L6
L5	l1 same l2 same l3	0	L5
L4	l1 and l2 and l3	96	L4
L3	hepes or mes or pipes	1210085	L3
L2	ammonium sulfate	39647	L2
L1	antithrombin III	2104	L1

END OF SEARCH HISTORY

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L7: Entry 7 of 8 File: DWPI Oct 4, 2001

DERWENT-ACC-NO: 2001-656912
DERWENT-WEEK: 200262

TITLE: New N-deacetylated, N-sulfated derivatives of K5 polysaccharide, useful as anticoagulant and antithrombotic agent, includes L-iduronic acid residues formed by epimerization

INVENTOR: ORESTE, P; ZOPPETTI, G ; CIPOLLETTI, G

PATENT-ASSIGNEE:

ASSIGNEE	CODE
INALCO SPA	INALN
ORESTE P	ORESI
ZOPPETTI G	ZOPPI

PRIORITY-DATA: 2000IT-MI00665 (March 30, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200172848 A1	October 4, 2001	E	038	C08B037/10
AU 200146510 A	October 8, 2001		000	C08B037/10
US 20020062019 A1	May 23, 2002		000	C12P019/04

DESIGNATED-STATES: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
WO 200172848A1	March 27, 2001	2001WO-EP03461	
AU 200146510A	March 27, 2001	2001AU-0046510	
AU 200146510A		WO 200172848	Based on
US20020062019A1	December 18, 2000	2000US-0738879	CIP of
US20020062019A1	September 12, 2001	2001US-0950003	

INT-CL (IPC): A61 K 31/715; C08 B 37/00; C08 B 37/10; C12 P 19/04

RELATED-ACC-NO: 2002-583547

ABSTRACTED-PUB-NO: US20020062019A
BASIC-ABSTRACT:

NOVELTY - N-deacetylated, N-sulfated derivative (I) of K5 polysaccharide that:

(a) is epimerized to at least 40% L-iduronic acid content (based on total uronic acids);

(b) has molecular weight 2-30 kD;

(c) contains 25-50 wt.% chains with high affinity for ATIII (antithrombin III); and

(d) has anticoagulant and antithrombotic activities characterized by HCII (heparin cofactor II) to anti-Xa ratio 1.5-4, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparing (I).

ACTIVITY - Anticoagulant; antithrombotic.

MECHANISM OF ACTION - Inhibition of thrombin. K5 polysaccharide (80% pure; 10 g) was purified by heat treatment and precipitation, then incubated for 18 hours at 60 deg. C in 2N sodium hydroxide for N-deacetylation and reacted with pyridine-sulfur trioxide complex (A) at 40 deg. C for N-sulfation. The product, as a desalted 10% solution, was dissolved in 25 mM Hepes buffer (pH 6.5) containing 50 mM calcium chloride (600 ml) and circulated, for 24 hours and at 200 ml/hour and 37 deg. C, through a column of immobilized glucuronosyl C-5 epimerase. The product has iduronic acid:glucuronic acid ratio 48:52. This was converted to its tetrabutylammonium (TBA) salt and supersulfated using (A). The product was converted to pyridine salt and treated with dimethylsulfoxide and methanol for selective 6-sulfation and then (after conversion back to TBA salt) with (A) for N-sulfation. The final product had, relative to UF heparin as 100%, 76.6% anti-Xa activity; 43.4% activated prothrombin time; 256% heparin cofactor II activity and 118% anti-IIa activity. Its antithrombin III affinity was 29%, compared to 32% for heparin, i.e. reduced overall anticoagulant activity but greater thrombin inhibition.

USE - (I) is useful as anticoagulant and antithrombotic agent.

ADVANTAGE - (I) has high anticoagulant and antithrombotic activities and fewer side effects (especially bleeding) than heparin.
ABSTRACTED-PUB-NO:

WO 200172848A
EQUIVALENT-ABSTRACTS:

NOVELTY - N-deacetylated, N-sulfated derivative (I) of K5 polysaccharide that:

(a) is epimerized to at least 40% L-iduronic acid content (based on total uronic acids);

(b) has molecular weight 2-30 kD;

(c) contains 25-50 wt.% chains with high affinity for ATIII (antithrombin III); and

(d) has anticoagulant and antithrombotic activities characterized by HCII (heparin cofactor II) to anti-Xa ratio 1.5-4, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for preparing (I).

ACTIVITY - Anticoagulant; antithrombotic.

MECHANISM OF ACTION - Inhibition of thrombin. K5 polysaccharide (80% pure; 10 g) was purified by heat treatment and precipitation, then incubated for 18 hours at 60 deg. C in 2N sodium hydroxide for N-deacetylation and reacted with pyridine-sulfur trioxide complex (A) at 40 deg. C for N-sulfation. The product, as a desalted 10% solution, was dissolved in 25 mM Hepes buffer (pH 6.5) containing 50 mM calcium chloride (600 ml) and circulated, for 24 hours and at 200 ml/hour and 37 deg. C, through a column of immobilized glucuronosyl C-5 epimerase. The product has iduronic acid:glucuronic acid ratio 48:52. This was converted to its tetrabutylammonium (TBA) salt and supersulfated using (A). The product was converted to pyridine salt and treated with

dimethylsulfoxide and methanol for selective 6-sulfation and then (after conversion back to TBA salt) with (A) for N-sulfation. The final product had, relative to UF heparin as 100%, 76.6% anti-Xa activity; 43.4% activated prothrombin time; 256% heparin cofactor II activity and 118% anti-IIa activity. Its antithrombin III affinity was 29%, compared to 32% for heparin, i.e. reduced overall anticoagulant activity but greater thrombin inhibition.

USE - (I) is useful as anticoagulant and antithrombotic agent.

ADVANTAGE - (I) has high anticoagulant and antithrombotic activities and fewer side effects (especially bleeding) than heparin.

CHOSEN-DRAWING: Dwg.0/11

TITLE-TERMS: NEW N N SULPHATED DERIVATIVE POLYSACCHARIDE USEFUL ANTICOAGULANT ANTITHROMBOTIC AGENT ACID RESIDUE FORMING

DERWENT-CLASS: A96 B04 D16

CPI-CODES: A03-A00A; A10-E01; A12-V01; B04-C02F; B14-F04; D05-A02; D05-C08;

CHEMICAL-CODES:

Chemical Indexing M1 *01*
Fragmentation Code
M423 M710 M720 M905 N134 N161 N422 P813 Q233
Specfic Compounds
A0121T A0121N A0121P

ENHANCED-POLYMER-INDEXING:
Polymer Index [1.1] 018 ; G3703 G3623 P0599 D01 ; M9999 M2835 ; L9999 L2391 ; L9999 L2835 ; M9999 M2346 ; M9999 M2788 ; L9999 L2346 ; L9999 L2788 ; M9999 M2313 ; L9999 L2313 Polymer Index [1.2] 018 ; ND01 ; ND06 ; B9999 B5094 B4977 B4740 ; Q9999 Q8037 Q7987 ; N9999 N6815 N6804 N6655 ; N9999 N6893 N6655 ; N9999 N6837 N6655 Polymer Index [1.3] 018 ; D01 D23 D22 D76 D41 D50 D61*R F20 N* 5A O* 6A S* ; H0226 Polymer Index [1.4] 018 ; S* 6A ; H0157

SECONDARY-ACC-NO:
CPI Secondary Accession Numbers: C2001-193268

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L7: Entry 2 of 8 File: USPT May 29, 2001

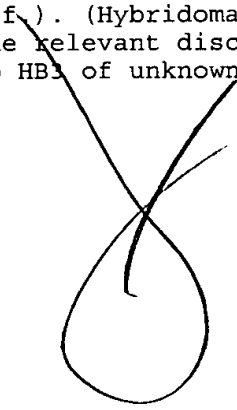
DOCUMENT-IDENTIFIER: US 6238875 B1
TITLE: Diagnostic methods useful in the characterization of lymphoproliferative disease characterized by increased EPR-1

Detailed Description Text (211):
The experimental procedures used for the isolation and purification of blood protease factor Xa were as described in Altieri, et al., J. Biol. Chem. 264, 2969 (1989)). Antithrombin III (ATIII, Sigma, St. Louis, Mo.) was used as a control irrelevant protein in lymphocyte proliferation experiments. Anti-CD3 mAb was OKT3; mAbs to .alpha./.beta. T cell receptor (WT-31), IL-2 receptor (1HT44H3), and to CD56 (Leu19) were purchased from Becton Dickinson (Mountain View, Calif.). Anti-.gamma./.DELTA.T cell receptor mAb .DELTA.-1 was generously provided by Dr. D. P. Dialynas (The Scripps Research Institute, La Jolla, Calif.). Anti-CD20 mAb B-1 was purchased from AMAC Inc. (Westbrook, Me.). Isotype-matched controls used in proliferation experiments were anti-CD57 mAb HNK-1 (IgM) (Abu, et al., J. Immunol. 129: 1758 (1982)), and two anti-tissue factor mAbs 9C6 and 5G9, generously provided by Dr. W. Ruf (The Scripps Research Institute, La Jolla, Calif.). (Hybridoma 5G9 is described in U.S. Pat. No. 5,110,730 to Edgington, et al., the relevant disclosures of which are incorporated by reference herein.) Non-binding mAb HB3 of unknown specificity was used as a control in flow cytometry experiments.

L7: Entry 3 of 8 File: USPT Jun 6, 2000

DOCUMENT-IDENTIFIER: US 6072028 A
TITLE: EPR-1 proteins, polypeptides, and nucleic acid molecules encoding same

Detailed Description Text (534):
The experimental procedures used for the isolation and purification of blood protease factor Xa were as described in Altieri, et al., J. Biol. Chem. 264, 2969 (1989)). Antithrombin III (ATIII, Sigma, St. Louis, Mo.) was used as a control irrelevant protein in lymphocyte proliferation experiments. Anti-CD3 mAb was OKT3; mAbs to .alpha./.beta. T cell receptor (WT-31), IL-2 receptor (1HT44H3), and to CD56 (Leu19) were purchased from Becton Dickinson (Mountain View, Calif.). Anti-.gamma./.DELTA. T cell receptor mAb .DELTA.-1 was generously provided by Dr. D. P. Dialynas (The Scripps Research Institute, La Jolla, Calif.). Anti-CD20 mAb B-1 was purchased from AMAC Inc. (Westbrook, Me.). Isotype-matched controls used in proliferation experiments were anti-CD57 mAb HNK-1 (IgM) (Abu, et al., J. Immunol. 129: 1758 (1982)), and two anti-tissue factor mAbs 9C6 and 5G9, generously provided by Dr. W. Ruf (The Scripps Research Institute, La Jolla, Calif.). (Hybridoma 5G9 is described in U.S. Pat. No. 5,110,730 to Edgington, et al., the relevant disclosures of which are incorporated by reference herein.) Non-binding mAb HB3 of unknown specificity was used as a control in flow cytometry experiments.



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L6: Entry 13 of 17 File: USPT Oct 25, 1983

DOCUMENT-IDENTIFIER: US 4411794 A
TITLE: Process for the purification of the blood clotting factors, II, VII, IX and/or X

Detailed Description Text (5):
The solution is brought to an ammonium sulfate concentration of 40 w/v %. The precipitate is centrifuged off and discarded. The supernatant is freed of sulfate ions by dialysis. Thereto there are added 0.25 kg of CaCl.sub.2.2H.sub.2 O and 0.25 kg of Ca.sub.3 (PO.sub.4).sub.2 and the product is stirred for 30 minutes at pH 7.6. Instead of 0.25 kg of Ca.sub.3 (PO.sub.4).sub.2, 1.3 liter of a 1 w/v % suspension of Al(OH).sub.3 may be used to obtain a comparable result. After centrifuging, the supernatant liquid is discarded and the adsorbent is washed with two 10 liter portions of 0.5 mol/l NaCl solution. The adsorbent is eluted with 1.8 liters of buffer at pH 8.0, which contains 0.2 mol/l of trisodium citrate, 0.15 mol/l of NaCl, 2 g/100 ml of glycine, 0.3 U/ml of antithrombin III and 14 IU/ml of heparin. After the addition of 0.2 g/100 ml of colloidal silica as a centrifuging aid, the eluate is separated from the adsorbent by centrifuging at 30,000 g. The residue is discarded and the supernatant liquid is dialyzed for 3 hours against 100 liters of a buffer at pH 7, containing 0.06 mol/l of NaCl, 0.02 mol/l of trisodium citrate and 2 g/100 ml of glycine. The dialyzate is tested for the activity of Factors II, VII, IX and X, is adjusted to the desired concentration, sterilized by filtration, divided into unit doses and lyophilized.

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L7: Entry 6 of 8 File: USPT Jul 20, 1993

DOCUMENT-IDENTIFIER: US 5229172 A
TITLE: Modification of polymeric surface by graft polymerization

Detailed Description Text (37):
Polyurethane samples made substantially as set forth in Example 2 were provided with covalently attached heparin by carbodiimide attachment. After overnight soaking of the samples in deionized water at 60.degree. C. to remove homopolymer, the grafted polyacrylamide surface was partially hydrolyzed by immersing the test samples in a 0.5M sodium carbonate buffer solution of pH=10.5 at 60.degree. C. for 2 hours. Then ethylene diamine was coupled to the surface by incubating the samples with a mixture of 0.5M ethylene diamine.2HCl and morpholineethanesulfonic acid (MES) with the pH adjusted to 5.0. 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) was added to effect coupling of the spacer molecule to the grafted surface. The test samples were immersed in an cold solution (ice bath) of 5 mg heparin (from porcine intestinal mucosa) per ml of buffer solution (0.5M MES; pH=5.0). Water soluble carbodiimide (EDC) was added to a concentration of 0.01M. The test samples were stirred in the solution at 0.degree. C. to 4.degree. C. for 6 hours. The solution was then decanted and the samples were thoroughly rinsed with cold deionized water, 1M NaCl, 1M NaHCO.sub.3, and deionized water. The test samples were then immersed in 1M NaHCO.sub.3 for 3 hours at 60.degree. C. followed by extensive rinsing with deionized water. The samples were then stored in 0.2M phosphate (pH=6.8) until bioactivity testing. Bioactivity testing was then conducted by determining the extent to which thrombin is deactivated by contact with the antithrombin III applied to the surface.

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L7: Entry 5 of 8 File: USPT Jun 16, 1998

DOCUMENT-IDENTIFIER: US 5767108 A
TITLE: Method for making improved heparinized biomaterials

Detailed Description Text (10):
The surface having immobilized heparin thereon is then provided with an adsorbed protein molecule which is capable of inhibiting the action of a blood coagulation protein to prevent coagulation of fibrinogen. By "protein molecule" we mean any naturally occurring protein or protein fragment which may be activated by heparin to inhibit the coagulation of fibrinogen. A preferred protein is antithrombin III which is known to be activated by heparin to inactivate thrombin. The protein can be adsorbed onto the surface with immobilized heparin immediately before the device is brought into contact with a patient's blood (e.g. by the surgeon immediately before a medical device is implanted) or, the immobilized heparin with adsorbed protein can be provided in a sterile device by drying the device with the immobilized heparin and adsorbed protein thereon and then packaging and sterilizing the device by conventional means. The protein can be easily bound to the heparinized surface by adsorption. For example, antithrombin III can be incubated in contact with a heparinized surface in a HEPES buffer solution for a few minutes followed by rinsing the surface to remove non-bound antithrombin.

Detailed Description Text (18):
This surface may be provided with antithrombin III by incubation for 15 minutes at 37.degree. C. with HEPES buffer with 500 nM antithrombin. The surface can then be washed to remove unbound antithrombin.

Detailed Description Text (23):
Some of the heparinized samples were provided with adsorbed antithrombin III by incubation for 15 minutes at 37.degree. C. with HEPES buffer and 500 nM antithrombin. The remaining heparinized samples were incubated in the same solution without antithrombin.

Detailed Description Text (25):
The test samples were incubated at 37.degree. C. in a platlet-rich plasma (citrated blood collected after venipuncture in the proportion of 1 part 0.12M trisodiumcitrate to 9 parts blood which was then centrifuged for 15 minutes at 250G at room temperature). Coagulation was started by adding CaCl.sub.2 (20 mM final concentration) to the plasma. At indicated time points, plasma was transferred into a cuvette with HEPES-EDTA and a thrombin substrate (S2238 from Chromogenics, Sweden). Results were as shown in FIG. 1. The surface with no heparin or antithrombin treatment indicated as curve 1 had an initial spike of thrombin. The surface with antithrombin treatment but no heparin indicated as curve 2 had an initial spike of thrombin that was substantially the same as that for curve 1. The surface with attached heparin but no antithrombin III indicated as curve 3 had no initial thrombin spike but in the 20-30 minute time span had an increase in thrombin production. The surface made according to the invention indicated by curve 4 remained flat throughout the measured time period, thus indicating no thrombin present in the test sample. Observation of the samples was consistent with these results with a clotting time for the heparinized sample of 18.3 minutes without antithrombin and no clotting at all noted during the 60 minute test for the sample with heparin and antithrombin.

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L7: Entry 4 of 8 File: USPT Dec 8, 1998

DOCUMENT-IDENTIFIER: US 5847084 A
TITLE: Process for obtaining platelet factor-4

Detailed Description Text (18):
Heparin (the final concentration of 7.2.times.10.sup.-3 units/ml; produced by Wako Pure Chemicals Ind., Ltd. of Japan), PF4 as obtained in Example 1 or produced by the conventional process), antithrombin III (the final concentration of 2.9 .mu.g/ml; produced by Seikagaku Kogyo Co. of Japan) and 40 mM HEPES (pH 7.4) were mixed to make the total volume of 2 ml, and the mixture was left on standing for 30 sec. at room temperature and admixed with 15 .mu.l of thrombin (the final concentration of 0.18 .mu.g/ml: produced by Sigma Co. of USA), followed by standing for 1 min at room temperature. After addition of Coloring Substrate S-2238 (the final concentration of 0.1 mM/ml: produced by Dai-Ichi Kagaku Co. of Japan), the degradation of the coloring substrate by thrombin was determined in a time-course manner by measurement of the absorbance at a wavelength of 405 nm.

L6: Entry 11 of 17 File: USPT Apr 9, 1985

DOCUMENT-IDENTIFIER: US 4510084 A
TITLE: Method of producing an antithrombin III-heparin concentrate or antithrombin III-heparinoid concentrate

Brief Summary Text (10):
According to an advantageous embodiment, the eluate is treated with protein precipitating agents, such as ammonium sulfate, in a concentration which suffices to precipitate the antithrombin III-heparin or antithrombin III-heparinoid complex, whereupon the precipitate is dissolved, the solution is thermally inactivated and the product is lyophilized thereafter. The thermal treatment for inactivating infection germs possibly present can be effected by heating to 60.degree. C. for a period of 10 hours.

Detailed Description Text (5):
From the combined eluates the antithrombin III-heparin complex was precipitated by adding 1.4 kg of ammonium sulfate and adjusting the pH to 5.5. The ammonium sulfate concentration of 430 g/l used herein corresponds to an 80% saturation of the solution. After stirring for one hour at +4.degree. C. the precipitate was separated by filtration and dissolved in 1.5 l of distilled water together with 13.5 g of NaCl and 221 g of Na.sub.3 citrate . 2H.sub.2 O.

CLAIMS:

6. A method as set forth in claim 5, wherein said protein precipitating agent for further treating said antithrombin III-heparin complex or antithrombin III-heparinoid complex is comprised of ammonium sulfate.

L6: Entry 16 of 17 File: USPT Jun 14, 1983

DOCUMENT-IDENTIFIER: US 4388232 A
TITLE: Method of producing plasma fractions free of side-effects using fast-reacting antithrombin

Detailed Description Text (82):
100 g immune globulin paste were dissolved in saline, i.e. a 0.9% sodium chloride solution, in the presence of 300 units of antithrombin III and 600 units of heparin to give a solution that contains 6.0 AT.sub.av -U/ml, and thereafter dialyzed. At 20.degree. C. 170 g/l ammonium sulfate were added, after separation of the precipitate the ammonium sulfate concentration of the supernatant was raised to 275 g/l to precipitate the purified immune globulin fraction. The latter was dissolved in saline, dialyzed and sterile-filtered after concentration by ultrafiltration.

Detailed Description Text (94):
To the eluate 22% polyethylene glycol 4,000 was added, the precipitate obtained was separated and discarded. By the addition of 28% polyethylene glycol the C1-esterase inhibitor was precipitated and separated. It was subjected to a further purification step. The precipitate was dissolved in saline containing 1,250 units of antithrombin III and 2,500 units of heparin, so that the solution contained 6.0 AT.sub.av -U/ml. The impurities were precipitated with the help of 310 g ammonium sulfate per liter, separated and discarded. The purified C1-esterase inhibitor was precipitated by the addition of 405 g/l ammonium sulfate from the supernatant, collected, dissolved in saline, dialyzed and sterile-filtered.

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L6: Entry 15 of 17 File: USPT Sep 13, 1983

DOCUMENT-IDENTIFIER: US 4404187 A
TITLE: Method for rendering factors II and VII hepatitis-safe with a chelating agent

Detailed Description Text (5):
After cooling, the mixture is diluted with 50 liters of distilled water and brought to an ammonium sulfate concentration of 40% weight/volume. The precipitate is centrifuged off and discarded. 0.5 kg of Ca phosphate are added to the supernatant liquid which is left to stand for 30 minutes at pH 7.6. After centrifuging, the supernatant liquid is discarded and the adsorbent is washed with twice 10 liters of 0.5 mole/l NaCl solution. The adsorbent is eluted with 1.8 liters of buffer of pH 8.0, which contains 0.2 mole/l of trisodium citrate, 0.15 mole/l of NaCl, 2 g/100 ml of glycine, 0.3 U/ml of antithrombin III and 14 IU/ml of heparin. After the addition of 0.2 g/100 ml of colloidal silica as a centrifuging aid, the eluate is separated from the adsorbent by centrifuging at 30,000 g. The residue is discarded and the supernatant liquid is dialyzed for 3 hours against 100 liters of a buffer of pH 7, containing 0.06 mole/l of NaCl, 0.02 mole/l of trisodium citrate and 2 g/100 ml of glycine. The dialyzate is tested for the activity of Factors II and VII, adjusted to the desired concentration, sterilized by filtration, divided into unit doses and lyophilized.

L6: Entry 14 of 17 File: USPT Sep 20, 1983

DOCUMENT-IDENTIFIER: US 4405603 A
TITLE: Method for rendering factors IX and X hepatitis-safe with calcium ions

Detailed Description Text (5):
The absorbent is eluted with 7.5 liters of 1 mole/l NaCl solution at pH 8.0 and is then discarded. 1.2 kg of glycine, 11.2 kg of sucrose and 0.55 kg of CaCl.sub.2.2H.sub.2 O are added to the eluate, and the mixture is heated for 10 hours at 60.degree. C. at pH 7.6. After cooling, the mixture is diluted with 50 liters of distilled water and brought to an ammonium sulfate concentration of 40% weight/volume. The precipitate is centrifuged off and discarded. 0.5 kg of Ca phosphate are added to the supernatant liquid which is left to stand for 30 minutes at pH 7.6. After centrifuging, the supernatant liquid is discarded and the adsorbent is washed with two 10 liter portions of 0.5 mole/l NaCl solution. The adsorbent is eluted with 1.8 liters of buffer of pH 8.0, which contains 0.2 mole/l of trisodium citrate, 0.15 mole/l of NaCl, 2 g/ 100 ml of glycine, 0.3 U/ml of antithrombin III and 14 IU/ml of heparin. After the addition of 0.2 g/100 ml of colloidal silica as a centrifuging aid, the eluate is separated from the adsorbent by centrifuging at 30,000 g. The residue is discarded and the supernatant liquid is dialyzed for 3 hours against 100 liters of a buffer of pH 7, containing 0.06 mole/l of NaCl, 0.02 mole/l of trisodium citrate and 2 g/100 ml of glycine. The dialyzate is tested for the activity of Factors IX and X, adjusted to the desired concentration, sterilized by filtration, divided into unit doses and lyophilized.

WEST

End of Result Set

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L6: Entry 17 of 17 File: USPT Oct 27, 1981

DOCUMENT-IDENTIFIER: US 4297344 A
TITLE: Blood coagulation factors and process for their manufacture

Brief Summary Text (51):
An antithrombin III preparation free from infectious virus is obtainable, for example according to the process as described by Andersson, L. K. et al. (German Auslegeschrift No. 2,243,688). To this end, dextran sulfate, heparin or chondroitin sulfate, alone or in the presence of agarose or of lysin-agarose, is rendered insoluble with cyanogen bromide by cross-linking in alkaline medium. After equilibrating of one of these materials in a chromatography column by means of an appropriate buffer, citrated plasma is absorbed thereon. The gel is washed until free of plasma and the antithrombin III-containing fraction is eluted using a buffer of higher molarity. If desired, the preparation is further purified by gel filtration through a molecular sieve. After concentration by precipitation with a neutral salt, preferably ammonium sulfate, the activity of the antithrombin III concentrate is determined.

Brief Summary Text (54):
To kill the hepatitis viruses, glycine and saccharose are added to the antithrombin III concentrate having the above characteristics in the manner described for factor VIII. After heating, any denaturized protein can be removed by centrifugation. The antithrombin III is concentrated by pressure dialysis or by reprecipitation with a neutral salt, preferably ammonium sulfate used in an amount from 50 to 80 w/v %, and further purified. For use in man, antithrombin III is dialyzed to have a physiological salt concentration, filtered under sterile conditions and optionally lyophilized for prolonged storage.

Detailed Description Text (30):
Upon passing through the column, the plasma has lost its coagulability. The column is washed with the original buffer and subsequently eluted by increasing the salt concentration stepwise to 1 mol/l NaCl.80 g of ammonium sulfate per 100 ml of solution are added to the eluate and the mixture is stirred for 2 hours. The precipitate formed is separated by centrifugation and taken up in 1 ml of distilled water. 1 g of saccharose and after complete dissolution thereof 0.3 g of glycine are added. The antithrombin-III-containing solution is heated for 10 hours to 60.degree. C.

Detailed Description Text (31):
After adding 4 ml of distilled water and 3 g of ammonium sulfate, the solution is left to stand for 18 hours, the antithrombin III-containing precipitate is submitted to centrifugation and taken up in 1 ml of physiological salt solution. Upon being dialyzed against a physiological salt solution, the preparation contains 1.6 units of antithrombin III per ml, which corresponds to an 80% yield.

WEST

End of Result Set

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L7: Entry 8 of 8 File: DWPI Aug 3, 1999

DERWENT-ACC-NO: 1999-488816
DERWENT-WEEK: 199944

TITLE: New medicinal composition composed of an effective ingredient of heavy specific gravity lipoprotein - useful for effective production of platelets and treatment of thrombocytopenia

PATENT-ASSIGNEE:

ASSIGNEE	CODE
ASAHI KASEI KOGYO KK	ASAH

PRIORITY-DATA: 1997JP-0319587 (November 20, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 11209399 A	August 3, 1999		000	C07K014/775

APPLICATION-DATA:

PUB-NO	APPL-DATE	APPL-NO	DESCRIPTOR
JP11209399A	May 28, 1998	1998JP-0146860	

INT-CL (IPC): A61 K 35/16; A61 K 38/00; C07 K 1/16; C07 K 14/775

ABSTRACTED-PUB-NO: JP11209399A
BASIC-ABSTRACT:

A new medicinal composition composed of an effective ingredient of a heavy specific gravity lipoprotein containing megakaryocytic projected alveolar forming activity, particularly non-absorptive in zinc chelating gel, especially containing antithrombin III, having C1 inhibitor activity, prepared by: (a) heating human blood at 60 deg. C for 10 minutes; (b) removal of protein to give a supernatant; (c) dialysis of the resultant supernatant against 10 mM NaOAc buffer at pH 4.5, to give a supernatant; (d) dialysis of the resultant supernatant against 10 mM HEPES buffer containing 150 mM NaCl at pH 7.4, to give a supernatant; (e) gel filtration with 10 mM HEPES buffer containing 150 mM NaCl at pH 7.4 to give a fraction having the activity; (f) contacting the active fraction with a zinc chelating gel under 10 mM HEPES buffer containing 150 mM NaCl at pH 7.4; (g) collection of non-absorptive fraction; (h) ultracentrifugation of the fraction adjusted to S.G. 1.21; and (i) collection of the floating yellow fraction to give the aimed heavy specific gravity lipoprotein containing megakaryocytic projected alveolar forming activity; used for treatment of thrombocytopenia. Also claimed is the heavy specific gravity lipoprotein having megakaryocytic projected alveolar forming activity and having following properties: (a) non-absorptive in a zinc chelating gel under 10 mM N-(2-hydroxyethyl)piperazine-N'-2-ethanes ulphonic acid (HEPES) buffer containing 150 mM NaCl at pH 7.4; (b) being fractionated at molecular wt. of 300 plus or minus 100 kd with gel filtration under 10 mM HEPES buffer containing 150 mM NaCl at pH 7.4; (c) fractionated at specific gravity of d = 1.2 or lower; (d) containing apolipoprotein A-I as a constituting protein; (e) capable of preparation of platelet; (f) containing

antithrombin III; and (g) containing CI inhibitor.

USE - The new composition is useful for effective production of platelets and treatment of thrombocytopenia.

CHOSEN-DRAWING: Dwg.0/11

TITLE-TERMS: NEW MEDICINE COMPOSITION COMPOSE EFFECT INGREDIENT HEAVY SPECIFIC GRAVITY LIPOPROTEIN USEFUL EFFECT PRODUCE PLATELET TREAT THROMBOCYTOPENIA

DERWENT-CLASS: B04

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